

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

National Institute of Dental and Craniofacial Research

National Advisory Dental and Craniofacial Research Council

Summary Minutes

Date: September 27, 2002

Place: Building 45, Conference Room E-1 & 2
National Institutes of Health
Bethesda, Maryland 20892

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

MINUTES OF THE
NATIONAL ADVISORY DENTAL AND CRANIOFACIAL RESEARCH COUNCIL

September 27, 2002

The 170th meeting of the National Advisory Dental and Craniofacial Research Council (NADCRC) was convened on September 27, 2002, at 8:30 a.m., in Building 45, Conference Room E-1 & 2, National Institutes of Health (NIH), Bethesda, Maryland. The meeting was open to the public from 8:30 a.m. to 12:05 p.m., followed by the closed session for Council business and consideration of grant applications from 1:00 p.m. until adjournment at 3:30 p.m. Dr. Lawrence A. Tabak presided as Chair.

Members Present:

Dr. Louise Chow
Dr. Nereyda Clark
Dr. Samuel F. Dworkin
Dr. Jay Alan Gershen
Dr. Howard Kuramitsu
Dr. Frank Macrina
Dr. Harold Morris
Dr. Linda C. Niessen
Dr. Joan Y. Reede
Dr. Dianne E. Rekow
Dr. Martha J. Somerman
Ms. Kim S. Urich

Members of the Public Present:

Mr. Jack Bresch, Associate Executive Director, American Dental Education Association (ADEA), Washington, DC
Dr. Nick Cavarocchi, CRD Associates, Washington, DC
Dr. Aida Chohayeb, Professor, Howard University, Washington, DC
Dr. Karl Haden, Associate Executive Director for Educational Policy and Research, ADEA, Washington, DC
Dr. John A. Klingensmith, Assistant Professor, Department of Cell Biology, Duke University, Durham, NC
Dr. Randy Kluender, ADEA, Washington, DC

Ms. Gina Luke, Director, State Government Relations and Advocacy Outreach, ADEA, Washington, DC
Dr. William Maas, Director, Division of Oral Health, Centers for Disease Control and Prevention, Chamblee, GA
Ms. Myla Moss, Director, Congressional Relations, ADEA, Washington, DC
Mr. Jonathan Schuermann, Ph.D. Candidate, University of Missouri, Columbia, MO
Dr. Louis Terracio, Associate Dean for Research, New York University College of Dentistry, New York, NY
Dr. Rick Valachovic, Executive Director, ADEA, Washington, DC

Federal Employees Present:

National Institute of Dental and Craniofacial Research:

Dr. Lawrence A. Tabak, Director, NIDCR
Dr. Dushanka V. Kleinman, Deputy Director, NIDCR
Dr. Margo Adesanya, Senior Scientist and Program Director, Clinical Trials and Patient-Oriented Research Program, Division of Population and Health Promotion Sciences (DPHPS)
Ms. Carolyn Baum, Committee Management Specialist and Council Secretary, Office of the Director (OD)
Dr. Henning Birkedal-Hansen, Scientific Director, NIDCR, and Director, Division of Intramural Research (DIR)
Dr. Norman S. Braveman, Assistant to the Director, OD
Dr. Patricia S. Bryant, Health Scientist Administrator and Program Director, Behavioral and Social Sciences Research Program, DPHPS
Ms. Jody Dove, Public Information Specialist, Public Information and Liaison Branch (PILB), Office of Communications and Health Education (OCHE)
Ms. Yvonne H. du Buy, Chief, Administrative Management Branch, Office of Administrative Management (OAM)
Dr. Caswell A. Evans, Director, National Oral Health Initiative, Office of the Surgeon General, and NIDCR
Dr. Isabel Garcia, Special Assistant for Science Transfer, OCHE, and Co-Director, NIDCR Residency Program in Dental Public Health
Dr. Sarah Glavin, Evaluation Officer, Office of Science Policy and Analysis (OSPA), OD
Dr. Sharon Gordon, Education Officer, OD
Dr. H. George Hausch, Acting Director, Division of Extramural Activities (DEA)
Ms. Lorraine Jackson, Extramural Research Coordinator and Outreach Specialist, DPHPS
Dr. Lynn King, Scientific Review Administrator, DEA
Dr. Eleni Kousvelari, Chief, Cellular and Molecular Biology, Physiology, and Biotechnology Branch, Division of Basic and Translational Sciences (DBTS)
Dr. James A. Lipton, Acting Deputy Director, DPHPS, and Director, Research Training and Career Development Program, DPHPS
Ms. Carol Loose, Budget Analyst, Financial Management Branch, OAM
Dr. Dennis F. Mangan, Chief, Infectious Diseases and Immunity Branch, DBTS

Dr. J. Ricardo Martinez, Executive Secretary, NADCRC, and Associate Director for Program Development, OD
Dr. Richard Mowery, Chief, Clinical, Epidemiology and Behavioral Research Branch, DPHPS
Dr. Ruth Nowjack-Raymer, Health Scientist Administrator and Program Director, Health Disparities Research Program, DPHPS
Dr. Bruce L. Pihlstrom, Acting Director, DPHPS
Dr. Ann L. Sandberg, Acting Director, DBTS
Dr. Yasaman Shirazi, Health Scientist Administrator and Program Director, Epithelial Cell Regulation and Transformation Program, DBTS
Dr. Rochelle Small, Health Scientist Administrator and Program Director, Developmental Biology and Mammalian Genetics Program, DBTS
Dr. Carolyn Tolbert, OSPA
Ms. Traci Walker, Committee Management Assistant, OD
Ms. Mary Ann Williamson, Computer Specialist, Office of Information Technology, OD
Dr. Guo H. Zhang, Health Scientist Administrator and Program Director, Physiology, Pharmacogenetics, and Injury Program, DBTS

Other Federal Employees:

Dr. Martin Brotemarkle, Office of Science Policy, Office of the Director, NIH, Bethesda, MD
Dr. Daniel Hickey, Legislative Chair, DePAC/Bureau of Prisons, El Paso, TX
Dr. Robert Mecklenburg, Consultant, National Cancer Institute, NIH
Dr. Lee Shackelford, Public Information Officer, DePAC/Indian Health Service, El Paso, TX
Ms. Sandra Talley, Program Analyst/Committee Management Officer, National Institute of Biomedical Imaging and Bioengineering (NIBIB), NIH, Bethesda, MD

OPEN PORTION OF THE MEETING

I. CALL TO ORDER

Dr. Lawrence A. Tabak, Director, NIDCR, called the meeting to order. He introduced three NIDCR staff members: Dr. Bruce L. Pihlstrom, who was recently appointed Acting Director, Division of Population and Health Promotion Sciences; Dr. Richard Mowery, who was recently appointed Chief, Clinical, Epidemiology and Behavioral Research Branch, Division of Population and Health Promotion Sciences; and Dr. Sharon Gordon, Education Officer, Office of the Director. Dr. Gordon organized a poster session for intramural postdoctoral fellows, which concluded the open portion of the Council meeting. Dr. Tabak noted that the theme of the meeting was research training and that the poster session provided an opportunity for postdoctoral fellows from each branch of NIDCR's Division of Intramural Research (DIR) to present their work.

Dr. Tabak invited all attendees to introduce themselves. He stated that the terms of four Council members were ending: Dr. John Alderete (who was unable to attend the meeting), Dr. Jay Gershen, Dr. Dianne Rekow, and Dr. Martha Somerman. Dr. Tabak thanked the

members for their contributions and presented each with a parting memento and a certificate of appreciation from the Secretary, Department of Health and Human Services. The three Council members attending the meeting thanked NIDCR for the opportunity to serve, commended NIDCR staff for their efforts, and urged NIDCR to disseminate information made available to the Council more widely to universities and all dental school deans. Dr. Tabak shared a letter from Dr. Alderete, who encouraged NIDCR to continue to seek advice from the extramural community, utilize the experience and energy of the Council, pursue the reduction of health disparities, and foster research training of underrepresented minorities.

II. APPROVAL OF MINUTES

The minutes of the Council's meeting on June 10, 2002, were considered and unanimously approved.

III. FUTURE COUNCIL MEETING DATES

The following dates for future Council meetings were confirmed:

February 3, 2003
June 16, 2003
September 19, 2003

January 20-21, 2004
May 24-25, 2004
September 27-28, 2004

IV. REPORT OF THE DIRECTOR

Dr. Tabak highlighted several items from the written Director's Report (see Attachment III).

Outreach. Dr. Tabak noted that he continues to reach out to schools and organizations to promote collaboration in dental, oral, and craniofacial research. In June, he gave a well-received presentation on "NIDCR's Strategic Directions for Priority-Driven Research and Training" at the Institute of Musculoskeletal Health and Arthritis of the Canadian Institutes of Health Research, an organization that is becoming the NIH equivalent in Canada. The purpose was to provide insight on NIDCR's planning and evaluation process.

Activities of the NIDCR Deputy Director. Dr. Tabak pointed out that the written Director's Report now includes a section on the activities of the Deputy Director. Since the previous Council's meeting, Dr. Dushanka V. Kleinman has made presentations to dental students, dental practitioners, community programs, and other audiences. In August, she participated in a site visit of Indian Health Service clinics in Montana which focused on discussions and program evaluation related to oral health, diabetes, and general health issues.

NIH Personnel. Dr. Tabak reported that Dr. Elias Zerhouni, Director, NIH, has named Dr. Thomas Insel as Director, National Institute of Mental Health, and that Dr. Insel is expected to begin his appointment in mid-November. Dr. Zerhouni also recently announced the appointment of Dr. Ting-Kai Li as Director, National Institute of Alcohol Abuse and Alcoholism. Dr. Tabak noted that NIDCR looks forward to working with both of these directors.

Meetings and Workshops. Dr. Tabak highlighted NIDCR's expert panels on scientific opportunities for 2004-09, which are being organized by Dr. J. Ricardo Martinez, Associate Director for Program Development. Two panels have already met to focus on Genomics and Proteomics and on Repair and Regeneration of Dental, Oral, and Craniofacial Tissues. A panel on Clinical Approaches to the Diagnosis, Treatment, and Prevention of Dental, Oral, and Craniofacial Disorders will be convened in October. Also, a panel on training has met to follow up on the NIDCR Blue Ribbon Panel on Research Training and Career Development to Meet Scientific Opportunities of the 21st Century, which was convened in 1999. Dr. Tabak noted that the products of the expert panels provide scientific underpinning for NIDCR's revision of its strategic plan and are displayed prominently on the Institute's website (see http://nidcr.cit.nih.gov/research/long_range_research_opps.asp).

On October 29, NIDCR will convene a workshop related to the Planning Awards to Enhance Research Infrastructure in Dental Schools. The workshop will be chaired by Dr. James A. Lipton, Director of NIDCR's Research Training and Career Development Program. It will be held at the NIH and include video conferencing for groups unable to come to NIH. The purpose is to address applicants' questions about the NIDCR Request for Applications (RFA) for these awards, which was issued on August 8. Applications are due on December 17.

NIH Road Map Initiative. Dr. Tabak reported that Dr. Zerhouni has initiated a process to develop a compelling vision for NIH activities over the next 3-5 years that promise the greatest impact on individuals' health. Inclusion of the extramural research community is an important part of this process. In August, NIH convened five meetings of scientists from NIH and the extramural community to identify the most important issues facing medical research, including the most promising opportunities and roadblocks. Dr. Tabak and Dr. Zerhouni co-chaired one of the meetings. Subsequently, the NIH leadership forum, which includes all institute and center (IC) directors, met to discuss and analyze the voluminous materials collected. Dr. Tabak noted several broad topical themes that have emerged: clinical research, interdisciplinary research, research resources and infrastructure, and new directions for research. He said that the process is continuing and further input will be sought.

Additional information on these and other NIDCR activities is provided in the written Director's Report (Attachment III).

V. UPDATE ON TRAINING AND MENTORSHIP

Dr. Martinez introduced the session on training and mentorship, which consisted of four presentations providing different perspectives on this issue. Dr. Tabak emphasized that research training is a very important arena of NIDCR activity.

Trainee Data

Dr. James A. Lipton presented a statistical "portrait" of research training supported by the NIDCR in recent years. Handouts provided to the Council contained additional detailed data. Dr. Lipton focused on two main categories of research training: National Research Service Awards (NRSAs), and research career development awards. For both categories, he summarized the number of awards and the funding of awards by specific mechanisms of support. He also related the percent of NRSA awards by primary research area, the success rates of applications for research training, and the percent and success rate of former awardees in obtaining a subsequent investigator-initiated R01 award.

Number and Funding of Awards. Preliminary data for FY 2002 show that NIDCR supported 31 institutional NRSAs. Approximately one-half (15) were comprehensive, multidisciplinary, institutional T32 NRSAs, which support training at all levels, and one-half (16) were traditional T32s. NIDCR initiated the comprehensive mechanism 2 years ago in response to recommendations from the 1999 NIDCR Blue Ribbon Panel and is phasing out the traditional T32s. NIDCR also supported 21 T35 short-term student awards (which also are being phased out); 9 individual postdoctoral fellowships (F32s); and 16 individual predoctoral dental scientist fellowships (D.D.S./Ph.D.) (F30s). Dr. Lipton said that the comprehensive T32 program is the most costly, averaging \$350,000 per award and totaling approximately \$5.3 million in FY 2002. The total cost for traditional T32s approximated \$1.2 million, and each of the other three award mechanisms cost less than \$1.0 million.

Turning to research career development awards, Dr. Lipton reported that NIDCR supported 10 Independent Scientist Awards (K02s). More popular mechanisms of support were the Mentored Clinical Scientist Development Award (K08, 13 awards); the NIDCR Scholar Development and Faculty Transition Award (K22, 19 awards) (the newest NIDCR mechanism); and the Mentored Patient-Oriented Research Career Development Award (K23, 21 awards). Other support included the Institutional Dentist Scientist Award (K16, 8 awards) and the Mid-Career Investigator Award in Patient-Oriented Research (K24, 6 awards). The two most well-funded programs were the K22 and K23.

Primary Research Areas. Dr. Lipton reported that, in FY 2002, the three most popular areas of training across all institutional NRSA (T32) awardees and individual NRSA (F30, F32) and research career development (K02, K08, K22, K23, K24) awardees were microbiology and microbial pathogenesis, immunology and immunotherapy, and biotechnology and biomaterials. He noted that a fair number of trainees in the institutional T32 programs also are being trained in population sciences research.

Success in Obtaining Research Training Awards. Dr. Lipton commented on the success rates of applicants to NIDCR training programs [success rate = number of awards divided by number of applications reviewed]. He noted that the success rates of NIDCR applicants for institutional and individual NRSA (T32s and F32s) and most research career development awards (K02, K08, K23) are similar to those across NIH. Two differences are apparent: Compared with NIH, NIDCR applicants are approximately twice as successful in obtaining K22 awards and slightly less successful in obtaining K24 awards.

Success in Obtaining Subsequent R01 Awards. NIDCR data on former NRSA trainees and research career development awardees for 1985-2000 show that, of all trainees receiving support during that time period, individual awardees [F32; Physician Scientist Award for Dentists (K11) and Individual Dentist Scientist Award (K15)] were far more successful (16.1 percent of all F32 awardees; 23.0 percent of all K11 and K15 awardees) in subsequently obtaining at least one R01 than were those participating in institutional awards (T32, K16) (4.3 percent of all T32 awardees, 7.8 percent of all K16 awardees). Dr. Lipton surmised that individuals who apply for research training support benefit from the rigorous experience of preparing and submitting an application, which is not gained by trainees who are selected by institutional programs.

Data on the success of R01 applications submitted by former NIDCR trainees and research career development awardees in obtaining R01 grants in 1985-2000 show similar results. The success rates [number of R01 awards divided by number of applications] of applications submitted by former trainees who had received individual research training awards (F32, K11, K15) were almost 2.5 times higher than for those who participated in institutional awards (T32, K16) (approximately 45 percent versus 18 percent). Dr. Lipton noted that these rates are quite competitive when compared with the overall success rate for type I (new, competitive) R01 awards at the NIH, which was approximately 26 percent in 2000 and ranged from 15.8 percent to 25.9 percent from 1990 through 2000.

Dr. Lipton noted further that the success rate of those former NIDCR trainees who submitted an R01 application was highest among former K11/K15 recipients (64 percent), followed by appointees to the K16 institutional Dentist Scientist Award (49 percent), F32 individual postdoctoral NRSA trainees (47 percent), and T32 institutional NRSA trainees (35 percent). Overall, the success rate of all former trainees/appointees was relatively high.

In discussion, Dr. Lipton said that former trainees often submit more than 1 application before they successfully obtain an R01 award. The number of applications submitted ranges from 3.2 (for former T32 awardees) to 2.0 (for former K11 and K15 awardees). The latter submit the fewest number of applications, but have the highest success rate. The number of R01 awards received ranges from 2.0 (for former F32 awardees) to 1.1 (for former K16 awardees). Dr. Lipton noted that F32 awardees are primarily Ph.D.s and that Ph.D.s generally submit fewer applications and have higher award rates.

The Council suggested additional types of data that would be useful for assessing the impact of NIDCR's training and career development program. These include the number of former trainees on dental school faculty, the number of former trainees conducting research, the percentage of all dental school faculty that received research training support from NIDCR, and the success rates

of trainees by gender and race. Dr. Lipton said that NIDCR will pursue these data, in collaboration with the American Dental Education Association (ADEA) and American Dental Association (ADA), as NIDCR constructs a database to track all NIDCR trainees retrospectively (to 1985) and prospectively.

Expert Panel

Dr. Martinez presented the recommendations of the NIDCR Training Panel, which met on June 7— a copy of the panel's full report was provided to the Council and is available at http://nidcr.cit.nih.gov/research/long_range_research_opps.asp. The panel addressed three topics: existing programs (specifically the T32 and T35); possible new programs (Lead Mentor Awards, Master's in Clinical Research), and training needs in emerging areas (genomics/proteomics, bioinformatics).

With regard to T32s, the NIDCR Training Panel recommended that NIDCR continue support for comprehensive institutional awards, identify broad areas of training needs, increase oversight and tracking of trainees, and encourage institutions that receive awards to focus on their strengths. With regard to T35s, the panel recommended that NIDCR phase out "stand-alone" programs; bundle T35s with the comprehensive T32s or Curriculum Development Awards (R25s); refocus the program so that trainees can only go to funded, active laboratories and research groups; and increase the programs' accountability for trainees' subsequent research activities.

The panel agreed with the concept of the two new awards proposed by NIDCR. For the Lead Mentor Award, which is intended as a mechanism for identifying and supporting outstanding scientists and mentors in specific areas, the panel recommended that NIDCR act as a broker between mentors and trainees, make a special effort to identify quality candidates, possibly limit initial awards to mentors of postdoctoral trainees, and offer incentives to mentors. For the Master's in Clinical Research, the panel recommended that NIDCR carefully define the criteria and expectations for the program, establish it as a pilot program initially, ensure critical oversight, engage dental schools' parent universities and sister medical schools, possibly link the program to K30 or T32 awards, and possibly make it a part-time program for junior faculty.

The panel offered six recommendations for training in emerging areas. The members suggested that NIDCR identify outstanding investigators and offer incentives to train individuals with dental background in emerging areas and technologies (e.g., genomics, bioinformatics); support short-term training models (possibly within the T32 program) to introduce dental students to emerging technologies and research advances; support long-term, intensive training models to develop a cadre of experienced investigators; offer training supplements to appropriate R01s; and link training opportunities to the Lead Mentor Award.

In discussion, Dr. Tabak reemphasized two points: the need for better tracking of NIDCR-supported trainees, and the requirement for increased accountability of training programs. In response to Council's observation of the need for training of Ph.D. investigators in clinical skills, he emphasized that NIH supports research training, not professional training, and that NIDCR's support of combined D.D.S./Ph.D. training has had mixed results. He agreed that alternative options need to be developed to expand the pool of clinical scientists and to help staff dental schools with research-trained faculty.

The Council suggested that the proposed Master's in Clinical Research program could be made available to non-dentist Ph.D. investigators who may be interested in clinical issues relevant to oral health research.

Mentoring

Dr. Joan Y. Reede, Dean, Diversity and Community Partnership, Harvard Medical School, Boston, Massachusetts, summarized the basics of mentoring, in a presentation she titled "Mentoring 101." She reviewed advantages that accrue to those who are mentored (mentees) and to mentors, concepts of mentoring, and responsibilities of mentors. She highlighted issues and responsibilities in mentoring individuals from two particular groups—minorities and women—and actions that institutions can take to improve mentoring.

Dr. Reede emphasized that mentoring is a "two-way street" of learning and exchange between mentors and mentees. Mentees gain enhanced knowledge sets and skills, recognition and encouragement, career advice, awareness of bureaucracy, and protection and advocacy within institutions. Mentors are able to update their knowledge and skills and their understanding of the values and perceptions of a younger generation and of changing career paths, reinforce their professional identity and worth, and establish a legacy. Individuals who pursue a "mentored maze" follow clear pathways leading to a goal, whereas those pursuing an "unmentored maze" face roadblocks, circular paths, and barriers blocking future progress.

Conceptually, mentoring may be informal or formal, include a continuum of short- to long-term relationships, involve multiple mentors (including peer and institutional mentors) who serve different roles at various stages of a mentee's career, and may be defined in many ways. In essence, mentoring is the process of building a relationship that evolves over time, reflects the goals of a mentee, and is based on mutual trust, understanding, and listening. Mentors must provide time for mentees, understand mentees' level of maturation and psychosocial development, serve as an intellectual guide and role model, provide challenge and validation, and be sensitive to differences between themselves and their mentees.

Dr. Reede noted that minorities and women share similar issues that, cumulatively, may "set them up" for failure in the scientific and medical environment. Specific issues for minorities relate to assumptions, stereotypes, undervaluation of individuals' scholarship, and perceptions of "token hires." Dr. Reede emphasized that these misperceptions carry through the entire academic system and, over time, have resulted in a limited number of role models and inadequate socialization for minorities. She noted that women are affected also by stereotyping, as well as other issues which relate to rank and compensation, promotion policies, isolation, modesty versus self-promotion, and less extensive informal networks. In addition, their career advancement is affected by other personal responsibilities and priorities.

Dr. Reede commented that the scientific and medical environment mirrors issues in the larger society, and she emphasized that mentors need to be cognizant of the types of issues facing minorities and women. When mentoring these individuals, mentors have a particular responsibility to open doors to challenging assignments, communicate that the mentee is a high performer, offer crucial advice and counseling about careers, provide sponsorship (e.g., visibility, opportunities for advancement), and

protect the mentee by confronting unfair criticisms. On their part, mentees should be mentorable, accept the mentor, enumerate their goals, seek advice, work hard, take initiative, and be committed to the mentoring process.

Dr. Reede highlighted two points: having an exceptional mentor does not guarantee promotion or success, and negative mentoring (both passive and active) does exist. She noted that institutions have a responsibility and can take action to improve the mentoring process. Their ability currently to improve mentoring is impeded by a general lack of recognition of the need for formal and informal mentoring, rewards for excellent mentoring, disincentives for poor mentoring, and actual mechanisms to improve mentoring.

Dr. Reede suggested that institutions could take four actions to improve mentoring: (i) acknowledge the importance of mentoring and encourage an institution's leaders to model good mentoring; (ii) integrate the monitoring and recognition of mentoring throughout the institution's system (e.g., through rewards, accountability, promotions, compensation); (iii) educate mentors and mentees and provide feedback to them on their performance; and (iv) profile successful mentoring. Dr. Reede noted that, six years ago, Harvard Medical School established a dean's mentoring award to visibly communicate the importance of mentoring throughout the institution. This award is now widely recognized and sought throughout the Harvard community. Mentors are nominated, and both nominees and awardees enjoy a larger presence at the school and often counsel others on good mentoring. Establishment of the award has led to broader discussions of the importance of mentoring and multiple advocates (offices and persons) for mentoring.

Enhancing Training in Clinical Research

Dr. Lipton presented two approaches envisaged by NIDCR for enhancing the cadre of well-trained investigators in clinical oral, dental, and craniofacial research. He noted that the dearth of well-trained clinical investigators, and particularly those with expertise in clinical trials, continues to be a major concern at the NIH, including NIDCR. Less than 20 percent of institutional NRSA programs and individual NRSA and research career development awards funded by NIDCR support training in clinical trials and patient-oriented research. To initiate discussion of this issue with the Council, NIDCR proposes two approaches for consideration.

Approach 1 is to improve collaboration with other ICs in order to increase dental clinicians' involvement in existing programs and activities and to take better advantage of two existing cofunding mechanisms [the Clinical Research Curriculum Award (K30) and the General Clinical Research Centers (GCRCs)]. Dr. Lipton noted that the purpose of the K30 award is to establish and improve didactic training programs in clinical research. Approximately 60 K30 programs are supported by NIH from cofunds contributed by the ICs, including NIDCR. Although 26 dental schools are located at U.S. institutions having K30 awards, relatively few of these schools participate in K30 activities at their institutions. Dr. Lipton noted that NIDCR also contributes to NIH support of approximately 78 GCRCs located throughout the United States, which provide an enriched environment for individuals conducting clinical research. Dentists, as well as physicians, are encouraged to participate in this activity, and 34 dental schools are located at sites holding a GCRC grant.

Approach 2 is to develop a new NIDCR program that would enhance training in clinical research. Dr. Lipton presented a summary list of issues that would need to be considered in developing such a program. For example, would funding be provided as an institutional or individual award? Could NIDCR leverage its existing contribution to the K30 program? Would support only be provided to institutions that have an established clinical research unit or expertise? Should trainees be pursuing a degree (e.g., M.S., Ph.D.)? Would candidates be limited to students or to junior or senior faculty? Would training be short- or long-term? What course work would be appropriate? And, would support be provided for advance specialty training?

In discussion, Dr. Tabak noted that clinical research, and particularly clinical trials, have become increasingly complex and sophisticated over the past 5-10 years and that traditional methods and curricula for clinical training embedded in most dental schools (e.g., leading to a Master's degree in orthodontics or oral medicine) are no longer sufficient. A more comprehensive, yet tailored and distributed, approach is needed that takes advantage of technological tools now available (e.g., teleinstruction, distance learning via the Internet). Master's-degree programs at Johns Hopkins University and Duke University, which can be accessed by trainees at other institutions, are two models. The type of program and award developed by NIDCR would need to be responsive to these new approaches to learning.

Commenting on the potential for increasing dental schools' participation in the K30 program, Dr. Lipton said that NIDCR contributes approximately \$300,000 each year to this program. Dr. Tabak noted that K30 awards are a trans-NIH initiative and that NIDCR would not be able to leverage individual awards, but could proactively educate and encourage institutions about this underused opportunity. He and Dr. Lipton noted further that K30 awards do not provide stipends or salary support for trainees and do not cover release time for faculty's training activities. These adjunct resources would need to be leveraged through other existing or new mechanisms.

The Council suggested that, to foster minority participation in clinical research, NIDCR could provide funding (e.g., through supplements) to leverage existing NIH support of centers of excellence in minority health and help to link dental schools to these centers within their institutions. The Council also commented on the question of who to train (students or faculty). Members noted the need for mechanisms to support training at both ends of the pipeline: that is, to attract students (at all levels) into dental, oral, and craniofacial research careers and to retain faculty by offering the incentive of support for additional training.

VI. UPDATE ON NEW INVESTIGATORS

Dr. Tabak informed the Council that NIDCR plans to provide periodic updates on NIDCR-supported new investigators, beginning with the Council's next meeting, which will be held in February 2003. The first update, which will reflect FY 2002 data, will provide the basis for comparing trends between new and experienced investigators. Dr. Tabak noted that this closer look at new investigators is precipitated by the phase out of the R29 (First Independent Research and Transition Award), which was succeeded by the R23 award (New Investigator Award), and a perception in the extramural community that new investigators are not being as successful as they could be in obtaining either a new or competing renewal R01 award. The data will be based on applicants' self-reports as new

investigators when they submit their NIH grant applications; a self-identifier was added to the application form in FY 2000. At Council's request, NIDCR will provide comparison with other IC data.

VII. UPDATE ON CONCEPT CLEARANCES AND ANNOUNCEMENTS

Dr. Martinez presented an update on concept clearances approved by the Council during the three review cycles for funding in FY 2002. He reported that NIDCR has issued 11 RFAs for 15 concepts and that action is pending on 4 concepts (which were approved by the Council at its June meeting). The science areas addressed include temporomandibular joint disorders (3 concepts); AIDS, biotechnology/bioengineering, health disparities, and research infrastructure (2 concepts each); and behavioral sciences, clinical research, genetics/developmental biology, and saliva/Sjögren's syndrome (1 concept each). For each review cycle, Dr. Martinez cited the list of concepts approved and the outcomes of each concept (date of announcement, due date of applications, and month of Council's second-level review).

In discussion, the Council commended NIDCR on the number and range of RFAs issued during FY 2002 and noted that they accentuate the mission of the Institute. The Council suggested that NIDCR distribute the list of concepts and outcomes more broadly to inform researchers and faculty of the totality of RFAs issued and to stimulate research grant applications. The Council specifically suggested that NIDCR disseminate this list to (a) all dental schools and academic health centers and (b) journals and newsletters of professional organizations such as the ADEA and American Association of Dental Research. The Council also encouraged NIDCR to highlight this information and make it more accessible on the NIDCR website.

VIII. RESEARCH PRESENTATION — "GETTING A HEAD IN THE MOUSE: MECHANISMS OF ROSTRAL DEVELOPMENT IN MAMMALS"

Dr. John A. Klingensmith, Assistant Professor of Cell Biology, Duke University, Durham, North Carolina, described his research on the roles of key signaling molecules in craniofacial development. Dr. Klingensmith, a developmental geneticist, received the Presidential Early Career Award for Scientists and Engineers (PECASE), given by President Bush on July 12 at a White House ceremony. Dr. Klingensmith is the first NIDCR new investigator to receive this award. His research is supported by NIDCR and the National Institute of Child Health and Human Development.

Dr. Klingensmith and colleagues are studying mechanisms that underlie development of the structures of the head, to better understand both normal development and craniofacial malformations. Using genetic technologies and mouse models, they are unraveling molecular and developmental pathways and relating them to clinical evidence. Dr. Klingensmith noted that the single greatest cause of infant mortality in the industrialized world is major congenital malformations (birth defects), which occur in approximately 1 in 50 live born babies. One-third of these defects involve craniofacial malformations, which include cleft palate, micrognathia, holoprosencephaly, and exencephaly. The holoprosencephaly (HPE) defect arises from a deletion of the rostral midline and can be extremely severe or subtle, occurring in as many as 1 in 250 conceptuses and about 1 in 1,000 live born babies.

Dr. Klingensmith noted that formation of the head is probably the most complex developmental process of all structures, including the brain, and that it precipitates from two centers, the brain and the rostral gut tube (which becomes the mouth). The head and the face are composed of many diverse tissues that interact to generate form and function, and this complexity is reflected in the variety, frequency, and severity of craniofacial malformations. Dr. Klingensmith described the formation of the head which occurs during two developmental stages, gastrulation and neurulation. He emphasized that the emergence of precursor tissues during gastrulation (at 21 days of human development) is the most important time in a person's life and the most sensitive period for environmental insults that could result in severe birth defects or death. The formation of ectoderm, endoderm, and mesoderm during gastrulation is followed by neurulation—including the formation of the neural crest cells and their migration to populate regions of the head. Dr. Klingensmith commented on the advantages of using mouse models to study these processes, noting that mice and humans share very similar genetic, developmental, and physiological mechanisms.

Significant studies of gastrulation began in the late 1920s, when researchers delineated, in tadpoles, the existence of an early and late "embryonic organizer" that induces the structures of the head and trunk, respectively. Using recombinant DNA tools, researchers were eventually able, in the 1990s, to identify secreted molecules that mimic this organizer activity. Two key molecules are chordin and noggin. These proteins are made in the organizer (the genes are expressed in the midline mesendoderm) and act antagonistically to other signals encoded by bone morphogenetic proteins (BMPs) made elsewhere in the early embryo.

Dr. Klingensmith elaborated on his research to delineate the specific roles of chordin and noggin in signaling and controlling craniofacial development. Utilizing genetic tools, he and his colleagues are conducting loss-of-function studies in four mutant classes of mice having various allele combinations of chordin and noggin. The results of these studies show various craniofacial effects related to mutations in the gene(s) for chordin and/or noggin. For example, lack of chordin results in a malformed head; lack of noggin results in abnormal neural tube formation; lack of both results in non-induction of a forebrain and a defective anterior visceral endoderm (AVE), the distinct organizer for the head in mice; and both chordin and noggin are needed, redundantly, for outgrowth of the mandible. The studies demonstrate that both chordin and noggin have critical roles in both the embryo organizer and the AVE. Further, their presence has implications for expression of fibroblast growth factor 8 (FGF8), which is needed for survival and proliferation of the neural crest, and BMPs, which promote apoptosis.

Dr. Klingensmith emphasized that complex heterozygotes of chordin and noggin are associated with various manifestations of defective rostral development (HPE), such as lack of an eye, nose, or jaw and cleft palate, and that the phenotypical results and outcomes in mouse models of HPE mirror those in human cases of HPE. Further, these craniofacial malformations are indication of neural malformations in the underlying neural structures, a finding that underpins a dogma in research on dysmorphologies, that "the face predicts the brain."

Dr. Klingensmith said that the mouse phenotypes also resemble very closely human phenotypes resulting from a heterozygous *Shh* gene. He noted that researchers have shown that most human HPE is due to mutations in this gene and that the outcomes depend on the nature of the gene defect—some

individuals die, and some live and are mildly or severely retarded. In studies to explore the connection between the mouse HPE phenotypes and the Shh gene, Dr. Klingensmith and colleagues have been able to show that chordin and noggin have a critical role in expression of this gene through their relationship with FGF8 and BMP. Studies are under way to determine specifically whether humans with HPE have mutations in the genes for chordin and noggin. Additional studies will be needed to explore the interaction of these genes with the Shh gene and other genes that may be identified. One key question is why the heterozygous Shh genotype results in a phenotype that varies dramatically in humans? Dr. Klingensmith suggested that outbred mice with a few bad alleles (i.e., heterozygous mutations in genes potentially associated with human HPE) could serve as a model for unraveling the complex genetics of human HPE. This research would extend the significant results obtained so far.

Dr. Tabak and the Council applauded Dr. Klingensmith for his elegant research and his ability to communicate complex science in an understandable way to other professionals and laypersons. The Council noted that his work is a good example of the full continuum of research and the transfer of results from bench science to clinical settings.

IX. POSTER SESSION — INTRAMURAL FELLOWS

Dr. Gordon invited the Council members to attend the poster session to speak with 10 postdoctoral fellows from DIR. The young scientists represented each DIR branch and discussed their posters. A booklet summarizing each poster and each fellow's background was available. The research presented covered the following 10 topics: differences in bone formation by human bone marrow stromal stem cells of different embryonic origin; the role of secretory leukocyte protease inhibitor (SLPI) in oral inflammation and tissue repair in the oral mucosa; the mechanism of action of perifosine, the only orally available alkylphospholipid for potentially treating a variety of human tumors; use of polymerase chain reaction-based cDNA subtraction to identify genes involved in the function of neuronal ganglia in normal and pathological conditions; the role of Kaposi's sarcoma herpesvirus (KSHV) in development of Kaposi's sarcoma; the ability of vanilloid receptor 1 agonists (e.g., capsaicin) to produce inactivation of peripheral nociceptive nerve endings, as an analgesic strategy for acute inflammatory pain; the activity of thymosin beta-4 in promoting wound repair and hair regeneration; the ability of human dental pulp stem cells to generate dentin-like tissue on human dentin; the role of the transient receptor potential (TRPC) family of ion channel proteins in the store-operated calcium entry (SOCE) mechanism of salivary gland cells; and signaling pathways and gene expression in macrophages infected with HIV-1.

CLOSED PORTION OF THE MEETING

This portion of the meeting was closed to the public in accordance with the determination that it was concerned with matters exempt from mandatory disclosure under Sections 552b(c)(4) and 552b(c)(6), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

There was a discussion of procedures and policies regarding voting and confidentiality of application materials, committee discussions, and recommendations. Members absented themselves from the meeting during discussion of and voting on applications from their own institutions, or other applications in which there was a potential conflict of interest, real or apparent. Members were asked to sign a statement to this effect.

VIII. REVIEW OF APPLICATIONS

Grant Review

The Council considered 444 applications requesting \$190,265,347 in total costs. The Council recommended 347 applications for a total cost of \$166,900,071 (see Attachment II).

ADJOURNMENT

The meeting was adjourned at 3:30 p.m. on September 27, 2002.

CERTIFICATION

I hereby certify that the foregoing minutes are accurate and complete.

Dr. Lawrence A. Tabak
Chairperson
National Advisory Dental and
Craniofacial Research Council

Dr. J. Ricardo Martinez
Executive Secretary
National Advisory Dental and
and Craniofacial Research Council

ATTACHMENTS

- I. Roster of Council Members
- II. Table of Council Actions
- III. Director's Report to the NADCRC, September 2002

NOTE: A complete set of open-portion handouts is available
from the Executive Secretary.